The Examiner has noted that there is an extra ")" in the specification at page 10, line 10. Applicant directs the Examiner's attention to the Amendment submitted February 16, 2000 wherein this typographical error has already been corrected.

The objection to the specification as allegedly containing terms that are trademarks and which are not properly noted, has been repeated. The Examiner has noted that the term "Nybond" on page 49, line 5 appears to be an error. Accordingly, Applicant has amended the specification to correct this typographical error and has replaced it with the term, "HYBOND®".

The terms "BioNick", "Photometric Cooled-CCD" and "RadPrime" are not registered trademarks. These terms were checked on Trademark-scan and also on the United States Patent Office's web site trademark search engine at http://tess.uspto.gov/bin/gate.exe?f=tess&state=6kqhtn.1.1 ("TESS") to determine if these terms were indeed registered. According to the results of these searches, the terms cited by the Examiner are apparently not registered trademarks. In addition, no actual evidence has been cited by the Examiner that these are in fact registered trademarks, e.g., registration numbers. As such, Applicant asserts that the request that these phrases be denoted as registered trademarks is improper and should be withdrawn.

## I. The Rejection Under 35 U.S.C. § 102(a), Should Be Withdrawn

Claims 1, 33-35, 38 and 41 are rejected under 35 U.S.C. § 102(a), as anticipated by Korenberg et al., 1994, Proc. Natl. Acad. Sci. 91:4997-5001 ("Korenberg"). Applicant respectfully traverses.

Korenberg merely describes the making of a map that correlates phenotypes of individuals with chromosome 21 trisomy with physical locations of human chromosomal markers by quantitative Southern blotting and fluorescent in situ hybridization using previously mapped chromosome 21 markers (see paragraph bridging page 4997 and 4998, as referenced by the Examiner). The goal of Korenberg is to identify regions of chromosome 21 that are associated with a given phenotype, which would facilitate positional cloning of genes that give rise to the phenotype.

The Examiner alleges that an inherent property of a product taught in Korenberg provides anticipation of the claimed invention of claim 1. With respect to claims 33-35, 38 and 41, the Examiner contends that "the isolated chromosomal DNA isolated for Southern

blot analysis" would be expected to hybridize to SEQ ID No.1. In response, Applicant points out that, in Korenberg, the chromosomal DNA that was isolated or purified from human cells was separated from the non-nucleic acid components of the cells, such that the chromosomal DNA was suitable for agarose gel electrophoresis. The isolated chromosomal DNA of Korenberg comprised all the genes in the human genome. In contrast, the isolated nucleic acid molecules of the invention exclude all the other genes and nucleic acids in the genome except the claimed nucleic acid molecules. Applicant does not dispute the fact the gene encoding DS-CAM was present in the human genomic DNA samples described in Korenberg. As the genomic DNA samples were taken from individuals with partial trisomies of chromosome 21, the gene encoding DS-CAM along with other genes on chromosome 21 were probably present in some samples at a higher copy number than other genes not located on chromosome 21. However, the fact remains that, in Korenberg, none of the claimed nucleic acid molecules were isolated or purified away from the rest of the genes in the genomic DNA sample. Applicant respectfully emphasizes that Korenberg does not teach or suggest any isolated nucleic acid molecules that would encode the recited polypeptides or hybridize to SEQ ID No. 1, 9, or 11 as recited because in Korenberg, the chromosomal DNA isolated from human cells for Southern blot analysis consisted of all the genes in the human genome. Thus, contrary to the Examiner's assertion, Korenberg does not disclose an isolated nucleic acid molecule that encodes the recited polypeptides or hybridizes to the recited nucleotide sequences, inherently or otherwise.

Moreover, on page 5001, column 1, last full paragraph, Korenberg states that the regions of interest on the chromosomes have not been cloned or isolated at all ("[w]hen the regions have been cloned in large fragment vectors such as yeast artificial chromosomes or bacterial artificial chromosomes, these agents may be used to isolate and evaluate genes that are expressed in human (or mouse) embryonic tissues"). Thus, Korenberg merely discusses a wish for having a cloned portion of the relevant chromosome in order to further identify genes in the identified chromosomal region, and does not teach any specific nucleic acid molecules that have been isolated and which contain nucleic acids within the scope of the presently claimed invention.

Applicant respectfully submits that the rejection under 35 U.S.C. § 102(a) is in error and requests that this rejection be withdrawn.

## II. The Rejection Under 35 U.S.C. § 102(b), Should Be Withdrawn

Claims 33-37, 47 and 48 are rejected under 35 U.S.C. § 102(b) as anticipated by GenBank Accession No. F13426. GenBank Accession No. F13426 teaches a nucleic acid of 309 base pairs encoding a polypeptide of 103 amino acids that is, according to the Examiner, 95.1% identical to the polypeptide of SEQ ID NO:2. Applicant respectfully disagrees for the following reasons.

The Examiner acknowledged that the nucleotide sequence of F13426 is not identical to and is merely similar to a portion of the claimed nucleic acid of SEQ ID NO:1. Applicant notes that F13426 corresponds to a segment of SEQ ID NO:1 that encodes a small portion of the cytoplasmic domain.

With respect to amended claim 33 which recites SEQ ID NO: 11, Applicant points out that SEQ ID NO:11 sets forth the amino acid sequence of a polypeptide that lacks the transmembrane and cytoplasmic domains of DS-CAM. As such, the region of similarity to F13426 is not present in SEQ ID NO:11, and therefore F13426 does not hybridize to any portion of the recited SEQ ID No. 11. Accordingly, F13426 does not anticipate the claimed nucleic acids of amended claim 33, inherently or otherwise. Applicant respectfully request the withdrawal of the rejection.

Furthermore, in view of the amendment of claims 34 and 35, Applicant respectfully submits that F13426 does not read on any of the claimed isolated nucleic acid molecules. The amended claims require that the claimed nucleic acid molecules hybridize separately to two segments of nucleotide sequences. Applicant submits that F13426 do not share sequence homology with the nucleotide sequences of the third nucleic acid in each of the amended claims, and thus would not hybridize to the recited nucleotide sequences under the recited hybridization stringency conditions. In view of the foregoing, Applicant further submits that claims dependent on claims 33, 34 or 35 are likewise not anticipated by F13426, inherently or otherwise.

In view of the foregoing, Applicant respectfully submits that these rejections have been overcome and/or obviated and request that the 35 U.S.C. § 102(b) rejection be withdrawn.

## III. The Rejection Under 35 U.S.C. § 103(a), Should Be Withdrawn

Claims 1, 31-43 and 49 are rejected under 35 U.S.C. § 103(a), as allegedly obvious in view of Korenberg in view of Gallatin et al., (US Patent No. 5,525,487; "Gallatin"). Claims 33-37 and 47-49 are rejected under 35 U.S.C. § 103(a), as allegedly obvious in view of GenBank Accession No. F13426 in view of Gallatin. The Examiner contends the claimed invention is obvious in view of the combined teachings of Korenberg or GenBank Accession No. F13426 and Gallatin, since Gallatin teaches methods of making a cell adhesion molecule polypeptide, DNA primers for amplification, radiolabeled oligonucleotides, etc.

Applicant respectfully disagrees with the rejections for the following reasons.

Firstly, as discussed at length above, there are no disclosures of the claimed isolated nucleic acid sequences in Korenberg, and thus, the Examiner's assertion that one of ordinary skill would have been motivated to use the DNA taught by Korenberg to express the DS-CAM protein is erroneous. There is no reasonable expectation of success in making the protein since no nucleic acid molecules encoding the protein had been isolated in Korenberg. Furthermore, there is no disclosure or suggestion of any cell adhesion molecules in Korenberg. Thus, there is no suggestion or motivation to combine Korenberg with Gallatin. Applicant respectfully submits that the rejection is in error and should be withdrawn.

Secondly, there is no teaching or suggestion that the sequence of GenBank Accession No. F13426 is located on Chromosome 21 or that it is related to cell adhesion molecules. The Genbank sequence does not encode a cellular adhesion molecule, such as taught by Gallatin or in the present invention, rather it merely teaches a nucleic acid fragment encoding a polypeptide fragment which has no known function. Thus, contrary to the Examiner's assertion, there is no motivation, absent the teachings of the present specification, to combine this sequence with the teachings of Gallatin to render the presently claimed invention obvious.

Moreover, there is no teaching or suggestion of the specific claimed nucleic acids of the invention in either GenBank Accession No. F13426 or Gallatin. The principle that the prior art must contain a suggestion of the desirability of the proposed combination of isolated disclosures in order to render an invention obvious is well known in patent law. Applicant submits that there is no motivation or suggestion to modify Gallatin or to combine it with the

GenBank sequence or Korenberg, as the Genbank sequence or Korenberg does not in itself provide any indication that F13426 or the genomic DNA sample encodes a cell adhesion molecule that is associated with a DS phenotype. Accordingly, in light of the above discussion, the combined teachings of Korenberg and Gallatin or F13426 and Gallatin can not and does not render obvious the claimed invention. The rejection under 35 U.S.C. § 103 should be withdrawn.

Furthermore, Applicant submits that the presently made rejection under § 103 is based on improper hindsight analysis gained from Applicant's own specification. Applicant respectfully reminds the Examiner that the Genbank sequence F13426 was identified by use of Applicant's sequence. Without the benefit of hindsight, the claimed invention could not have been foreseen by a person of ordinary skill in the art, since there was no teaching or suggestion in the art. As noted in the response filed February 16, 2000, hindsight is not permitted to deprecate the inventive steps taken by an inventor in deriving an invention.

Thus, in view of the above-made arguments and amendments, Applicant respectfully requests that the rejection under 35 U.S.C. § 103(a) be withdrawn.

## CONCLUSION

Applicant respectfully requests that the amendments of the present response be entered and made of record in the instant application. An allowance of the claims is earnestly requested. Applicant believes that each ground for rejection or objection has been successfully overcome or obviated and that the application is in condition for allowance. If any issues remain in connection herewith, the Examiner is respectfully invited to telephone the undersigned to discuss the same.

Respectfully submitted,

Date: November 8, 2000

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Enclosures

**Exhibit A**

Pending Claims for
Application Serial No. 08/956,991
as of November 8, 2000

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1. An isolated nucleic acid comprising (a) a nucleotide sequence encoding a polypeptide comprising the amino acid sequence of SEQ ID NO:2 or 11; and (b) the complement of the nucleotide sequence of (a).

31. A vector comprising the isolated nucleic acid of claim 1.

32. An isolated cell containing the nucleic acid of claim 1 or 31.

33. An isolated intronless nucleic acid comprising a nucleotide sequence which hybridizes under high stringency conditions to a second nucleic acid encoding the amino acid sequence set forth in SEQ ID NO:11, wherein said high stringency conditions comprise hybridizing in 5X Denhardt's solution, 5X SSPE and 0.2% sodium dodecylsulfate at 42°C, followed by washing in 0.1X SSPE and 0.1% Sodium dodecylsulfate at 65°C.

34. An isolated nucleic acid that hybridizes under high stringency conditions to a second nucleic acid consisting of the nucleotide sequence set forth in SEQ ID NO:1 that encodes amino acids 24 to 126 of SEQ ID NO:2 and a third nucleic acid consisting of the nucleotide sequence set forth in SEQ ID NO:1 that encodes amino acids 1069 to 1185 of SEQ ID NO:2, wherein said high stringency conditions comprise hybridizing in 5X Denhardt's solution, 5X SSPE and 0.2% sodium dodecylsulfate at 42°C, followed by washing in 0.1X SSPE and 0.1% Sodium dodecylsulfate at 65°C.

35. An isolated nucleic acid comprising a nucleotide sequence which hybridizes under high stringency conditions to a second nucleic acid consisting of the nucleotide sequence set forth in SEQ ID NO:7 or SEQ ID NO:8, wherein said high stringency conditions comprise hybridizing in 5X Denhardt's solution, 5X SSPE and 0.2% sodium dodecylsulfate at 42°C, followed by washing in 0.1X SSPE and 0.1% Sodium dodecylsulfate at 65°C.

36. A vector comprising the isolated nucleic acid of claim 33, 34, or 35.

37. An isolated cell containing the nucleic acid of claim 33, 34, or 35.

38. An isolated nucleic acid comprising a nucleotide sequence which encodes a polypeptide comprising at least one of the amino acid sequences selected from the group consisting of: amino acids 1-23, 24-126, 127-225, 226-316, 317-409, 410-506, 507-603, 604-697, 698-792, 793-887, 888-983, 984-1067, 1068-1185, 1186-1281, 1282-1375, 1376-1471, 1472-1594, 1595-1616, and 1617-1910 of SEQ ID NO:2.

39. A vector comprising the isolated nucleic acid of claim 38.

40. An isolated cell containing the nucleic acid of claim 38 or 39.

41. An isolated nucleic acid molecule comprising a nucleotide sequence set forth in SEQ ID NO:1, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, nucleotides 453-6185 of SEQ ID NO:1 or nucleotides 453-5168 of SEQ ID NO:1.

42. A vector comprising the isolated nucleic acid of claim 41.

43. An isolated cell containing the nucleic acid of claim 41 or 42.

44. An oligonucleotide comprising at least 15 nucleotides of (a) a nucleotide sequence that encodes the polypeptide of SEQ ID NO:11; (b) the nucleotide sequence set forth in SEQ ID NO. 7 or 8; or (c) the complement of the nucleotide sequence of (a) or (b).

45. The oligonucleotide of claim 44 wherein the oligonucleotide sequence consists essentially of SEQ ID NO:5 or SEQ ID NO:6.

46. A kit for detecting the presence of a nucleic acid in a sample comprising in a package at least one oligonucleotide of claims 44 or 45.

47. The isolated nucleic acid of claim 1, 33, 34, 35, 38 or 41 which is cDNA.

48. The isolated nucleic acid of claim 1, 33, 34, 35, 38 or 41 which is RNA.

49. A method for making of a Down Syndrome-Cell Adhesion Molecule polypeptide or fragment thereof, said method comprising the steps of culturing the cell of claim 32, 37, 40 or 43 under conditions suitable for expression of said Down Syndrome-Cell Adhesion Molecule protein, and isolating the expressed Down Syndrome-Cell Adhesion Molecule protein.